2014-5073

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

VALERIA FLORES,

Petitioner-Appellant,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent-Appellee.

Appeal from a judgment of the United States Court of Federal Claims
in Case No. 10-VV-489, JUDGE MARGARET M. SWEENEY

BRIEF OF RESPONDENT-APPELLEE SECRETARY OF HEALTH AND HUMAN SERVICES

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STATEMENT OF RELATED CASES

No appeal of this case has been before this or any other appellate court. To the knowledge of respondent-appellee, the Secretary of Health and Human Services ("the Secretary"), there is no same or similar Vaccine Act case pending before the Supreme Court, this Court, or any other Circuit Court of Appeals.

COUNTER-STATEMENT OF THE ISSUE

Did the Special Master apply the correct legal standards and properly exercise his discretion in determining that petitioner-appellant, Valeria Flores ("petitioner") failed to prove by preponderant evidence that her human papillomavirus ("HPV") vaccinations caused her to develop a spinal cord stroke.

STATEMENT OF THE CASE

I. Nature of the Case.

This is a case brought under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 ("Vaccine Act" or "Act"), *as amended*, seeking compensation for an injury, a spinal cord stroke, that is not listed on the Vaccine Injury Table ("Table"). Petitioner was required to prove by preponderant evidence that the HPV vaccine caused her spinal cord stroke, in order to receive compensation under the Act.

II. Statutory Scheme: National Childhood Vaccine Injury Act.

In 1986, Congress passed the Vaccine Act, establishing a program administered by the Secretary of Health and Human Services to increase the safety and availability of vaccines. See 42 U.S.C. § 300aa-1; Terran v. HHS, 195 F.3d 1302, 1307 (Fed. Cir. 1999). The Vaccine Act created the National Vaccine Injury Compensation Program, through which claimants could petition to receive compensation for vaccine-related injuries or death. See 42 U.S.C. § 300aa-10(a). The Vaccine Act establishes an Office of Special Masters within the United States Court of Federal Claims ("CFC") to issue decisions on petitions for compensation (42 U.S.C. §§ 300aa-12(c)(1), 300aa-12(d)(3)(A)), provides for review of a special master's decision by the CFC (42 U.S.C. § 300aa-12(e)), and allows appeal of the CFC's rulings to this Court. 42 U.S.C. § 300aa-12(f).

To receive compensation, a claimant petitions the CFC and must show, by preponderant evidence, that the vaccinated person received a covered vaccine and either: (1) suffered an injury or condition or a significant aggravation of a pre-existing injury or condition listed on the Table within the requisite time frame, in which case causation is presumed (a "Table injury"); or (2) suffered an injury or condition or suffered the significant aggravation of a pre-existing injury or

condition not on the Table, in which case causation must be proven (an "off-Table injury"). See id. at §§ 300aa-11(c)(1)(C), 300aa-14; 42 C.F.R. § 100.3 (2008).

The facts here did not support a Table injury, and petitioner agrees that she cannot establish one. Thus, compensation is awarded only if the fact finder concludes "that the petitioner has demonstrated by a preponderance of the evidence" entitlement to compensation, and also holds "that there is not a preponderance of the evidence" showing that the injuries were "due to factors unrelated to the administration of the vaccine." 42 U.S.C. §§ 300aa-13(a)(1)(A), 300aa-13(a)(1)(B); see Hines v. HHS, 940 F.2d 1518, 1524-25 (Fed. Cir. 1991). To prove actual causation of an off-Table injury, petitioner needed to:

> show by preponderant evidence that the vaccination brought about [petitioner's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between the vaccination and the injury.

Moberly v. HHS, 592 F.3d 1315, 1322 (Fed. Cir. 2010) (quoting Althen v. HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005)). All three prongs of the Althen test must be satisfied by preponderant evidence. de Bazan v. HHS, 539 F.3d 1347, 1351-52 (Fed. Cir. 2008); Caves v. HHS, 100 Fed. Cl. 119, 132 (2011), aff'd per curiam, 463 Fed. App'x. 932 (Fed. Cir. 2012) (finding that "[w]hen a petitioner seeks to

demonstrate causation in fact by meeting the three Althen requirements, each of those requirements must be proven by a preponderance of the evidence").

Petitioner was not required to prove her case to a level of scientific certainty. Rather,

> the burden of showing something by a "preponderance of the evidence," the most common standard in the civil law, simply requires the trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the [judge] of the fact's existence.

Moberly, 592 F.3d at 1322 n.2 (quoting Concrete Pipe & Prods. of Cal., Inc. v. Constr. Laborers Pension Trust for S. Cal., 508 U.S. 602, 622 (1993)).

Under the preponderance standard, the special master was required to assess the reliability of petitioner's scientific evidence by looking for sound and reliable medical or scientific support. Moberly, 592 F.3d at 1325 ("[W]e have made clear that the special masters have that responsibility in Vaccine Act cases.") (citations omitted); see also Rules of the United States Court of Federal Claims ("RCFC"), Appendix B, Vaccine Rule 8(b)(1) (instructing special masters to consider only "relevant and reliable evidence"). "Simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." LaLonde v. HHS, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing Moberly, 592 F.3d at 1322).

This Court has repeatedly approved the use of the Daubert factors[1] as a tool or framework to determine the reliability of the evidence in Vaccine Act cases, even though the Federal Rules of Evidence do not set the standards for the admission of evidence under the Act.

III. Course of Proceedings and Disposition in the Court Below.

The relevant procedural history is set forth in the Special Master's Decision and is not in dispute. See Appendix at 7 (hereinafter referred to as "A_ "). Petitioner's father filed a petition on her behalf on July 29, 2010. A7, A28.[2] Thereafter, petitioner filed medical records and an expert report from a neurologist, Douglas Kerr, M.D. A7, A28. The Secretary filed her Vaccine Rule 4(c) report on December 30, 2010, recommending that compensation be denied, along with an expert report from Peter Bingham, M.D., a pediatric neurologist. A7, A28, A132-

[1] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 589-90 (1993). In Daubert, the Supreme Court listed factors that a trial court can use in evaluating an expert's opinion: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and, (4) whether the theory or technique enjoys general acceptance within a relevant scientific community. Terran, 195 F.3d at 1316 n.2 (citing Daubert, 509 U.S. at 592-95).

[2] During the pendency of this claim, Valeria Flores reached the age of majority and was substituted as the petitioner on January 30, 2013. A28. For the sake of clarity, the term "petitioner" shall refer to filings made both by Valeria Flores and her father, while he was petitioner on behalf of Valeria Flores.

37. On February 21, 2011, petitioner filed a responsive expert report from Dr. Kerr. A7, A28. On May 25, 2011, the Secretary filed an expert report from Joan Gill, M.D., a pediatric hematologist. A7, A28, A293-96. Both parties filed medical literature. A hearing was held on January 31, 2012. Thereafter, the parties submitted post-hearing briefs. A7, A28. On September 12, 2013, the Special Master issued a 25-page Decision, concluding that petitioner failed to prove her claim by preponderant evidence. A1-25. The Special Master detailed his findings discussing spinal cord strokes, and he also discussed petitioner's pre- and post-vaccination medical history, the reports and testimony from Drs. Kerr, Bingham, and Gill, and the medical literature filed by both parties. In denying the claim, the Special Master found that petitioner did not meet her burden on any prong of the Althen test. A2, A7-8, A22-25.

On October 14, 2013, petitioner timely moved for review of the Special Master's Decision. On February 26, 2014, in a 13-page Decision, Judge Sweeney affirmed the Special Master's Decision. A26-38. Specifically, in denying the motion for review, Judge Sweeney reviewed petitioner's assertion that the Special Master erred as a matter of law or otherwise abused his discretion in finding that petitioner was unable to establish her burden of proof under Althen. Judge Sweeney reviewed, in detail, each of petitioner's challenges, and found that, aside

from one error – which she determined to be harmless – the Special Master properly considered the relevant evidence, acted appropriately in reviewing the evidence, and applied the proper burden of proof. A29-38. This appeal followed.

STATEMENT OF THE FACTS

I. Medical Facts

The Secretary adopts the facts set forth in the Special Master's and the CFC's Decisions. A4-6, A27. Briefly, petitioner, who was fourteen years old at the time of her alleged injury, received HPV vaccinations on April 28, 2008, and June 27, 2008. A4, A27. Early in the day on June 28, 2008, the day after her second HPV vaccination, petitioner developed a headache and left-sided weakness that quickly progressed to shortness of breath, which prompted her family to call 911.[3] Id. During transport to the hospital, petitioner developed bradycardia and suffered a cardiac arrest. Id. She was resuscitated and intubated and was awake at the time she arrived at Mt. Sinai Hospital emergency room ("Mt. Sinai"). A6.

Upon arrival at Mt. Sinai, petitioner was unable to move her extremities. A4. She was immediately tested for signs of inflammation or blood coagulation

[3] The precise time petitioner's symptoms began on June 28, 2008 is not clear. A4. There is no dispute, however, that petitioner's symptoms began before 12:30 p.m. on June 28 and quickly progressed to quadrapalegia with ventilator dependence. Id.

(blood clotting) in order to determine the etiology for her condition. A5, A10, A15-16, A37. A complete blood count ("CBC") was performed and all markers of inflammation – white blood cells ("WBC"), platelets, and neutrophils – were within normal limits. A5, A10, A14, A37, A683. A platelet test, which can provide evidence of a clotting condition, was also normal. A5, A683-84. Petitioner was assessed with acute respiratory failure and transferred to Rush Hospital ("Rush") for further evaluation. A5, A27.

At Rush, petitioner's medical doctors strongly suspected that her correct diagnosis was either transverse myelitis ("TM") or a spinal cord stroke, and she was again tested for signs of systemic inflammation or coagulation.[4] A5, A27. Tests for inflammation, including C-reactive protein ("CRP") and sedimentation ("Sed") rate, were negative. A5, A687-88. Coagulopathy tests, including: prothrombin and PT-INR, Protein S and C, and Antithrombin III deficiency, were also normal. A5, A689-90. Several D-dimers, very sensitive tests for venous

[4] A spinal cord stroke occurs when there is a blockage in the spine that prevents blood flow through the spine and causes tissue death due to a lack of oxygen. A7. A spinal cord stroke is also known as a spinal cord "infarct" or "infarction." Id. In this case, all experts agreed that petitioner's stroke was most likely caused by a blood clot that became lodged in a spinal cord vessel. Id. A blood clot that causes a stroke is also called a "thrombus." Id.

thrombosis (a condition where a person forms a blood clot in a vein), were also normal.[5] A13, A35-36. Other genetic tests for Factor V Leiden and Prothrombin gene mutations were negative. A5. Petitioner tested positive for a MTHFR-1298 gene mutation, but her homocysteine level was normal. A5, A12, A32, A694-96.

After extensive testing, petitioner's treating neurologists opined that her condition was more likely caused by a spinal cord stroke rather than TM. A5-6 (citing A685). The first, Dr. Tilwalii, noted that petitioner's lack of inflammatory markers, lack of response to anti-inflammatory treatment, "history of paralysis occurring over 15 minutes, [and] MRI C[ervical] cord demonstrating a lesion in anterior cord strongly suggests a vascular etiology – a spinal cord infarct." Id. He also noted that petitioner's "vaccination 1 day prior is too close to onset of [symptoms] to induce an inflammatory response." Id. The second, Dr. Stefofski, noted that petitioner's rapid onset in symptoms "strongly favors a vascular etiology over immune mediated/inflammatory (definitely too soon for [her HPV vaccine to be a] myelitogenic trigger)." A6 (citing A686). While most of petitioner's treating doctors were aware that she received an HPV vaccine the day before her symptoms

[5] Two D-dimer tests were administered on July 5, 2008. A691-92. The results were .51 and .46. Id. A third D-dimer was administered on July 6, 2008, and the result was .49. A693. All were within normal limits.

began, none who suspected petitioner's correct diagnosis was a spinal cord stroke opined that her vaccination caused her injury.

II. Experts

At hearing, the Secretary called two experts and petitioner called one. Petitioner's expert was Dr. Douglas Kerr, a board-certified neurologist and physiatrist. A8. He currently works as the Director for neurodegeneration research at Biogen-Idec, a biotechnology company. Id. Prior to that, he served as an associate professor of neurology, molecular biology, and immunology at Johns Hopkins School of Medicine and School of Public Health. Id. He also previously served as director of the Johns Hopkins Transverse Myelopathy Center.[6] Id. Dr. Kerr opined that petitioner's HPV vaccinations on April 28 and June 27, 2008, caused her to suffer a spinal cord stroke on June 28, 2008. A8-9, A28. He opined that petitioner has a "genetic predisposition" that made her susceptible to blood clotting, and that her HPV vaccines caused an "exuberant" and rapid systemic

[6] In her brief, petitioner mentions that Dr. Kerr once testified on behalf of the Secretary in vaccine-injury compensation claims. Flores Brief at 22-23. While Dr. Kerr has previously testified for the Secretary, he has not testified for the Secretary since 2010, when he left Johns Hopkins University after the University determined that he had engaged in professional and research misconduct. A8.

immune response that either caused systemic inflammation or coagulation, which resulted in a blood clot that caused petitioner's stroke.[7] A9, A28.

The Secretary's first expert was Dr. Joan Gill, who is board-certified in pediatrics, pediatric hematology, and oncology. A10, A706-47. Her medical practice focuses entirely on the care of children with blood disorders. A10. She is a professor of pediatric medicine and epidemiology at the Medical College of Wisconsin. Id. She is also an Investigator at the Blood Center of Southwest Wisconsin. Id. For the last twenty-five years, Dr. Gill has directed a treatment program where she cares for over 1,000 patients, including children, who have genetic predispositions for bleeding and clotting conditions, and immune-mediated hematological disorders. A10, A441. Notably, Dr. Gill was the only hematologist who testified in this case.

Dr. Gill opined that petitioner's only known genetic abnormality, a methylenetetrahydratefolate reductase A1298C ("MTHFR-1298") heterozygous mutation, is not associated with clotting conditions and did not cause petitioner's blood clot that led to her stroke. A10-12. She also testified that she was not aware

[7] Dr. Kerr initially presented a third theory, that petitioner's vaccinations caused her to develop an antiphospholipid syndrome that caused her to develop a blood clot. A9. However, when shown lab results that petitioner tested negative for antibodies associated with this syndrome, he abandoned this theory at hearing. A9, A446-47.

of any method by which an HPV vaccination could cause the development of blood clots that could lead to a spinal cord stroke. A10. She explained the clinical evidence did not support Dr. Kerr's theories, because if Dr. Kerr's theories were correct, petitioner's diagnostic testing should have demonstrated some clinical evidence of inflammation or coagulation immediately following the onset of her stroke; however, petitioner's testing revealed no such abnormalities. A10-12, A14-16.

The Secretary's second expert was Dr. Peter Bingham, a board-certified pediatric neurologist. A9, A699-705. Dr. Bingham is an associate professor of pediatrics and neurology at the University of Vermont and is board-certified in neurology and physiatry. A9. He is a member of the American Academy of Neurology and Child Neurology and Professor of Child Neurology. Id. Dr. Bingham runs a neurology clinic, treats children with a wide range of neurological problems, and conducts clinical research in the area of neuromuscular disease. Id.

While Dr. Bingham agreed that petitioner's correct diagnosis was a spinal cord stroke, he disagreed with Dr. Kerr's theories and explained that petitioner's diagnostic tests did not support Dr. Kerr's theories. A10. Dr. Bingham also testified that there is no known association between the HPV vaccination and

spinal cord strokes or blood clot formation that could lead to a stroke. Id. Finally, he opined that petitioner's vaccines were not a probable cause of her stroke. Id.

SUMMARY OF THE ARGUMENT

Petitioner claims that her receipt of HPV vaccines caused her to suffer a spinal cord stroke. On the basis of a voluminous record, including medical expert witness reports and testimony for both sides, the Special Master carefully considered the competing scientific evidence and concluded that petitioner did not carry her burden to show actual causation. The Special Master applied the correct evidentiary standard and stated a rational basis for his conclusion that petitioner failed to support her claim with preponderant evidence. The Special Master evaluated all of the relevant evidence and determined that petitioner had not established a reliable medical theory under Althen prong one causally connecting petitioner's HPV vaccines to her spinal cord stroke. The Special Master further determined that petitioner lacked preponderant evidence on Althen prongs two and three. These determinations are amply supported by the evidence and are entitled to significant deference under this Court's precedent. Indeed, Judge Sweeney carefully reviewed the Special Master's Decision, and discerned no reversible legal error with regard to the Special Master's evaluation of the evidence or his well-

supported determinations. Accordingly, the Decisions of the Special Master and the CFC should be affirmed.

STANDARD OF REVIEW

This Court reviews *de novo* a ruling by the CFC on a special master's decision to grant or deny entitlement to compensation under the Vaccine Act. Lampe v. HHS, 219 F.3d 1357, 1360 (Fed. Cir. 2000) (citing Bradley v. HHS, 991 F.2d 1570, 1574 (Fed. Cir. 1993)). Whether the special master applied the appropriate standard of causation is a legal determination reviewed by this Court *de novo* under the "not in accordance with law" standard. See Munn v. HHS, 970 F.2d 863, 870-73 (Fed. Cir. 1992). However, this Court is to apply the arbitrary and capricious standard to fact findings, and the special master's discretionary rulings are to be reviewed under the abuse of discretion standard. Id. at 870 n.10. As this Court has held:

> Congress assigned a group of specialists, the Special Masters within the Court of Federal Claims, the unenviable job of sorting through these painful cases and, based upon their accumulated expertise in the field, judging the merits of the individual claims. The statute makes clear that, on review, the Court of Federal Claims is not to second guess the Special Master's fact-intensive conclusions; the standard of review is uniquely deferential for what is essentially a judicial process. Our cases make clear that, on review . . . we remain equally deferential. That level of deference is especially apt in a case in which the medical evidence of causation is in dispute.

Hodges v. HHS, 9 F.3d 958, 961 (Fed. Cir. 1993) (internal citations omitted). Thus, this Court does "not reweigh the factual evidence, assess whether the special master correctly evaluated the evidence, or examine the probative value of the evidence or the credibility of the witnesses – these are all matters within the purview of the fact finder." Porter v. HHS, 663 F.3d 1242, 1249 (Fed. Cir. 2011) (citing Broekelschen v. HHS, 618 F.3d 1339, 1349 (Fed. Cir. 2010)). As long as a special master's factual findings are "based on evidence in the record that [is] not wholly implausible, we are compelled to uphold that finding as not being arbitrary and capricious." Cedillo v. HHS, 617 F.3d 1328, 1338 (Fed. Cir. 2010) (citing Lampe, 219 F.3d 1363). As this Court recently noted, "[t]he arbitrary and capricious standard provides a fact finder the most deference possible." Paterek v. HHS, 527 Fed. App'x. 875, 881 (Fed. Cir. 2013) (citing Munn, 970 F. 2d at 870). Thus, reversible error is "extremely difficult to demonstrate" if the special master "has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision." Hines, 940 F.2d at 1528.

ARGUMENT

I. The Special Master applied the correct legal and evidentiary standards to petitioner's off-Table injury claim.

As shown below, the Special Master fully considered the record as a whole, and applied the correct legal and evidentiary standards in reaching his Decision to dismiss petitioner's claim.

A. The Special Master applied the correct legal standard with regard to *Althen* prong one and correctly found that petitioner failed to provide a reliable medical theory connecting petitioner's vaccination and injury.

The Special Master makes clear in his Decision that the Althen test was the appropriate framework for his causation-in-fact analysis, and Judge Sweeney correctly held that the Special Master properly applied that standard. A2-3, A22-24, A38. Petitioner agrees that the Althen test applies to her causation-in-fact claim. Flores Brief at 4-5.

Petitioner, however, in an attempt to demonstrate error, mischaracterizes her legal burden of proof. At the outset, petitioner argues that her burden under Althen prong one is satisfied by simply positing a "plausible medical theory." Flores Brief at 6, 18, 21, 38. This Court, however, has repeatedly rejected this argument and held that petitioner must do more than demonstrate a "plausible" or "possible" link between a vaccination and an alleged injury; petitioner must instead prove

each element of her claim by preponderant evidence. Moberly, 592 F.3d 1322 n.2; see also LaLonde, 746 F.3d at 1339 (the statutory standard requires more than just proof of a "plausible" or "possible" causal link between the vaccine and the injury (citation omitted)); W.C. v. HHS, 704 F.3d 1352, 1356 (Fed. Cir. 2013) ("petitioner must do more than demonstrate a 'plausible' or 'possible' causal link between the vaccination and the injury").[8] Here, the Special Master made clear that, in accordance with the law, he held petitioner only to the preponderance standard for each element of her claim. A2-3, A7, A22-23.

Additionally, contrary to petitioner's assertions, the Special Master did not require petitioner to produce evidence of a "precise mechanism of injury." Flores Brief at 56. Instead, he carefully reviewed the reliability of the two theories proposed by petitioner's expert: 1) that the HPV vaccine can cause spinal cord strokes via inflammation, and 2) that the HPV vaccine can cause blood clots that can cause spinal cord strokes; and found that neither theory was supported by reliable, preponderant evidence. The underlying record reflects that the Special Master fully considered the record as a whole, including the testimony of all the experts, when he found that petitioner had not satisfied her burden.

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[8] Petitioner did not reference any of these recent cases in her brief.

Petitioner also argues, for the first time, that the Special Master committed an error of law under Andreu, by "fram[ing] his rejection of Dr. Kerr's causation theory under the rubric of a credibility determination." Flores Brief at 55 (citing Andreu v. HHS, 569 F.3d 1367 (Fed. Cir. 2009)). She further states that the Special Master committed "a pattern whereby [he] distorts what Dr. Kerr said, clearly misunderstood it, or, having determined that Dr. Kerr was engaging in sheer speculation, arbitrarily and uncritically dismissed it[.]" Id. at 36, 50, 54-60. This legal argument should be disregarded, as petitioner is prohibited from raising issues for the first time in this appeal. Weddel v. HHS, 23 F.3d 388, 390 n.2 (Fed. Cir. 1994) (noting that any "argument not raised specifically in the record before the special master shall be considered waived"); Jay v. HHS, 998 F.2d 979, 983 (Fed. Cir. 1993). However, even if this Court were to determine this issue is properly before it, the Special Master did not err in his consideration of the expert testimony.

This case is a quintessential battle of the experts. As the finder of fact, the Special Master was responsible for weighing the persuasiveness of the parties' evidence. In weighing the evidence, special masters "are entitled – indeed, expected – to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting the

evidence." Moberly, 592 F.3d at 1326. "Assessments as to the reliability of expert testimony often turn on credibility determinations, particularly in cases . . . where there is little supporting evidence for the expert's opinion." Id. A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." Id. at 1324 (citing Terran, 195 F.3d at 1316). This Court's opinion in Andreu only prohibits a special master from requiring a petitioner to satisfy a heightened burden of proof, while framing his rejection of petitioner's evidence as a credibility determination. 569 F.3d at 1379. But that is not what occurred here. The Special Master did not invoke a credibility determination as his reason for finding Dr. Kerr's opinion unpersuasive, and Andreu, simply does not apply.

Here, the Special Master properly evaluated the expert testimony under the correct legal standard and Judge Sweeney affirmed his findings. A29-38. A review of the underlying record makes clear that the Special Master found Dr. Kerr to be a qualified expert with "prestigious academic credentials" who offered sincere testimony. A8 n.10. The Special Master noted, however, after review of the record as a whole, that the opinions of Drs. Gill and Bingham were "substantially more persuasive than that of Dr. Kerr in this case" and that Dr. Kerr

was unable to establish a reliable basis for his opinion under the preponderance standard. A8 n.10, A25.

Finally, petitioner asserts that the Special Master erred as a matter of law by considering the literature submitted by the parties to support his decision. Flores Brief at 9, 45-47, 56. It is important to note that the Special Master did not require petitioner to submit medical literature to support her claim. A20. Indeed, he noted that "petitioner need not supply epidemiological or other medical literature supporting causation." Id. (citing Capizzano v. HHS, 440 F.3d 1317, 1325 (Fed. Cir. 2006); Andreu, 569 F.3d at 1378). A special master, however, is allowed to consider epidemiologic and medical literature once it is placed into the record, and the Federal Circuit has consistently upheld a special master's finding that an expert's theory was unreliable, in part, because medical literature filed in the case failed to support it. See LaLonde, 746 F.3d at 1341 (noting that "petitioners must proffer trustworthy testimony from experts who can find support for their theories in medical literature in order to show causation under the preponderance of evidence standard"); W.C., 704 F.3d at 1360-61; Locane v. HHS, 685 F.3d 1375, 1380 (Fed. Cir. 2012); Porter, 663 F.3d at 1253-55. The Secretary can also offer epidemiological evidence or literature when it contradicts a petitioner's theory. Stone v. HHS, 676 F.3d 1373, 1379-80 (Fed. Cir. 2012), reh'g en banc denied, 690

F.3d 1380 (Fed. Cir. 2012), cert. denied, 133 S.Ct. 2022 (2013); de Bazan, 539 F.3d at 1353. As such, it was entirely appropriate for the Special Master to consider the literature filed in this case when evaluating the reliability of petitioner's medical theories.

1. Petitioner did not provide reliable evidence to establish that she has a "genetic predisposition" for a bleeding or blood clotting condition that could result in a spinal cord stroke.

Dr. Kerr *unequivocally* premised both of his theories of causation – that petitioner's HPV vaccinations caused either inflammation or platelet aggregation that resulted in her stroke – on the *vital condition precedent* that petitioner *must have* a "genetic predisposition" likely involving a combination of several genes that would predispose her to a vaccine reaction. A10-11. He emphasized that this genetic predisposition was "absolutely critical" to his theories, but failed to provide any evidence that petitioner had this genetic predisposition. Id.

As a legal issue, the Secretary recognizes that petitioner is not required to prove her case to a level of scientific certainty, and this Court has held that a petitioner can establish her burden via circumstantial evidence. Althen, 418 F.3d at 1280. The Secretary, however, respectfully disagrees with Judge Sweeney that it was error for the Special Master to find that petitioner failed to establish

preponderant evidence that she had a genetic abnormality that would predispose her to clotting. A33.

As a matter of law the special master must require petitioner to support each element of her claim by preponderant evidence, beyond "speculation or guesswork." A11; see Moberly, 542 F.3d at 1322. Preponderant evidence requires a fact finder to "believe that the existence of a fact is more probable than it's nonexistence before [he] may find in favor of the party who has the burden to persuade the [judge] of the fact's existence." Id. at 1322 n.2 (quoting Concrete Pipe & Prods. of Cal, Inc., 508 U.S. at 622.

Here, petitioner argues that she is not required to produce any evidence, other than an unsupported statement from her expert that she has a genetic predisposition, in order to establish a portion of her medical theory. Flores Brief at 35. Indeed, she acknowledges that Dr. Kerr offered absolutely no direct evidence on this point when she notes that when testifying regarding her alleged genetic mutation, "Dr. Kerr was only observing that some form of genetic loading, a genetic predisposition, is necessary and therefore critical in order for an individual to suffer a rare reaction." Id. When asked what other genetic abnormality petitioner had that, when combined with her HPV vaccination, would cause her to develop a spinal cord stroke, Dr. Kerr responded that he did not know. A11. At no

time did Dr. Kerr testify that there was other evidence in the medical record that would support a genetically-mediated clotting condition. Instead, he simply testified that in the absence of genetic loading, petitioner would not have suffered a vaccine injury. A350-51. As such, petitioner essentially argues that she is entitled to a presumption that she has a genetic abnormality. This position, however, is contrary to law because a court, in evaluating a causation-in-fact claim, cannot grant a petitioner any presumptions in favor of causation.

A review of the evidence presented on this issue demonstrates that petitioner did not demonstrate via either direct evidence (genetic test results) *or* circumstantial evidence (such as other clinical test results) that she had a genetic abnormality that predisposed her to a vaccine injury. A10-12. The Special Master correctly noted that prior to hearing, Dr. Kerr's expert report unequivocally stated that he had identified a genetic mutation in petitioner that, when combined with her HPV vaccinations, caused her to develop her spinal cord stroke – a MTHFR-1298 mutation. A11, A70-71. However, at hearing, Dr. Kerr backed away from that assertion. A11, A391 (when Dr. Kerr was asked at hearing if he thought petitioner's MTHFR-1298 mutation alone could have "predisposed her" to a stroke, Dr. Kerr responded, "No. It is my testimony that it is not that, that . . . is not a critical factor").

Moreover, while Dr. Kerr offered two articles that discussed blood clotting conditions in people with some variants of MTHFR mutations, neither addressed the MTHFR-1298 mutation. A11-12. The Special Master correctly concluded that because the literature relied upon by Dr. Kerr did not relate to the mutation petitioner actually has, it was not persuasive. Id.

Indeed, Dr. Gill, who commonly treats patients with genetically-mediated bleeding and clotting conditions, explained that petitioner's MTHFR-1298 mutation does not cause blood clotting.[9] A11. She explained that MTHFR mutations can only confer a risk of clotting through increased homocysteine production. A11-12. She explained that while some variants of the MTHFR genes might increase homocysteine production (which in turn leads to blood clotting), the 1298 variant does not. Id. She submitted a published, peer-reviewed article that explained that the MTHFR-1298 mutation is harmless and does not lead to increased homocysteine production. A11, A748-53. Dr. Gill also explained petitioner's blood work showed normal homocysteine levels, which provided

[9] Dr. Gill was the only hematologist who testified in this case, and her level of expertise was acknowledged by Dr. Kerr when he stated that while he could diagnose a patient with a spinal cord stroke, he would defer to a hematologist to determine the cause of the clot. A11 n.13.

further evidence that her MTHFR-1298 mutation, or any other genetic variant of MTHFR, played absolutely no role in her spinal cord stroke. A11.

Based on this evidence, the Special Master correctly concluded that "Dr. Kerr totally failed to establish a factor that he himself called a 'critical factor' in his analysis – that [petitioner] had some type of *genetic predisposition* that made her susceptible to have blood clots." A12. Because Dr. Kerr could not provide a reliable basis for his opinion that petitioner's only known genetic mutation, MTHFR-1298, could cause a stroke, or any evidence (either direct or circumstantial) that petitioner had another mutation that could cause clotting, the Special Master correctly found that Dr. Kerr's opinion on this "critical factor" amounted to nothing more than "sheer speculation." Id. He also correctly concluded that because Dr. Kerr's theories were premised on an alleged "genetic predisposition," petitioner could not prevail on either of her theories. Id. Despite this conclusion, the Special Master still fully analyzed the remaining portions of petitioner's theories and found them equally unsupported by reliable evidence.

2. The Special Master did not abuse his discretion when he determined that petitioner's stroke was arterial rather than venous.

Portions of Dr. Kerr's theories were also premised on an assumption that petitioner suffered a venous stroke. The Special Master carefully considered the

record as a whole, including the testimony of all the testifying experts, when he concluded that petitioner's stroke was arterial rather than venous. A12-13. The Special Master simply found Dr. Gill's explanation of the differences between these two types of strokes to be more persuasive, particularly given her expertise in bleeding and clotting disorders. A12. Judge Sweeney also reviewed this evidence and determined that "the special master's decision reflects that he considered the testimony of all three experts regarding the bases for their respective positions, as well as [the submitted medical literature]." A35. Judge Sweeney concluded that the Special Master did not abuse his discretion in the manner in which he evaluated the evidence. Id. She also noted that simply because the "special master assigned different weights to this evidence than the weights preferred by petitioner is not an abuse of discretion."[10] Id.

The Special Master correctly noted that arterial and venous strokes are different. A12. Arterial strokes occur in arteries, while venous strokes occur in

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[10] Petitioner argues that Dr. Kerr's opinions should have been sufficient to establish petitioner's burden because he has treated more spinal cord stroke patients than Dr. Gill. Flores Brief at 50-51. However, Judge Sweeney evaluated this argument and noted that this point is not determinative because it is "only one aspect of what the special master could have considered in analyzing the origins of petitioner's blood clot." A35. Petitioner's brief fails to note that Dr. Gill's professional career focuses entirely on treating children with bleeding and clotting conditions. A441-44.

veins. Id. Dr. Gill explained that arteries deliver fully oxygenated blood to the spinal tissue, and veins, in contrast, function to take the deoxygenated blood back to the lungs and heart where it is reoxygenated. A12, A447. She explained that if a clot occurs in an artery, an injury can happen fairly rapidly and can result in a "medical emergency." A12, A446-47. If a clot occurs in a vein, "the blood that gets into the spinal cord cannot be drained . . . and it's this kind of back flow pressure that ultimately causes the spinal cord to die." A354, A447. She explained that venous clots generally cause a backup of blood prior to reaching the obstruction, and often a patient experiences swelling and pain over several days. A447.

The Special Master noted that while Dr. Kerr disagreed with Dr. Gill's testimony, Dr. Kerr did not offer a coherent explanation for this disagreement. As petitioner correctly notes in her brief, "Dr. Kerr did not know whether the blood clot was venous or arterial," but he relied quite heavily on medical literature that discussed venous strokes (or venous thromboembolisms) to support his opinions in this case.[11] Flores Brief at 26; A17-19. While Dr. Kerr explained that if a clot became lodged in a vein at the "exactly right" place, it could cause a devastating

[11] See *infra* Section I(A)5, discussion of Barbara Slade, et. al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine,* JAMA (2009) 302:750 ("Slade article") (A297-305).

injury as quickly as petitioner's injury, he never testified that petitioner's injury occurred at *that particular spot,* nor did he submit any additional evidence that venous strokes can present similarly to petitioner's stroke.[12] A12, A556.

To help resolve this dispute, the Special Master carefully reviewed the only article submitted regarding the clinical course of arterial strokes, the "Novy article."[13] A12-13. That study followed 27 people who suffered arterial spinal cord strokes, and every one of those patients suffered a sudden onset in symptoms exactly like petitioner. A12. Indeed, the Novy authors explained that every patient suffered a sudden onset of neurological symptoms, with symptoms proceeding from non-existent to very serious "usually within about 2 minutes," but always within "a few hours." A12, A152. The authors also explained that unlike the sudden onset in arterial strokes, a venous spinal cord stroke usually follows a "subacute progressive course." A13, A156. The Special Master noted that this

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[12] In her brief, petitioner discusses research from two French neurologists "Dr. Foix and Dr. Alajouanine," referenced by Dr. Kerr at hearing when discussing this particular testimony. Flores Brief at 28. However, Dr. Kerr did not submit this research for consideration by the Court.

[13] Jan Novy, et. al. *Spinal cord ischemia – clinical and imaging patterns, pathogenesis, and outcomes in 27 patients*. 63 Arch. Neurol. (2006) 1113. A150-57.

article directly supported the testimony of Dr. Gill and made her opinions more persuasive. A13.

Finally, and most importantly, the Special Master explained that petitioner's medical tests *showed no evidence of a venous stroke*. A13. In particular, petitioner underwent several D-dimer tests, which Dr. Gill explained is a "very sensitive test," for venous thrombosis. A13, A481. Indeed, Dr. Gill testified that "if you have a negative D-dimer, it's very, very unlikely that you have a venous thromboembolic event." A481. All of petitioner's D-Dimer tests were within normal limits. A691-93. Petitioner did not submit any evidence to rebut Dr. Gill's interpretation of these studies. After careful review of this evidence, Judge Sweeney found that it was not improper for the Special Master to credit Dr. Gill's testimony over that of Dr. Kerr. A36.

3. Petitioner did not provide a reliable medical theory explaining how an HPV vaccination can cause inflammation that can lead to a spinal cord stroke.

The Special Master also appropriately concluded that Dr. Kerr failed to provide preponderant evidence that the HPV vaccination can cause systemic inflammation that would, in turn, cause a blood clot that would lead to a spinal cord stroke. A13-15. Dr. Kerr's testimony made clear that this entire theory rested on the premise that petitioner's second HPV vaccination caused "massive

microglial activation" that led to inflammation that resulted in a spinal cord stroke. A13. Dr. Kerr conceded, however, that he did not know if the HPV vaccination would even cause microglial activation.[14] A13. He also conceded that under this proposed theory, he did not know how much inflammation would be necessary to cause a stroke, whether that inflammation could be tested, or for how long it would persist after a vaccination.[15] A376-77. Absent any reliable evidence that the HPV vaccine could even trigger the type of inflammation proposed by Dr. Kerr, the Special Master correctly concluded that Dr. Kerr's theory was not reliable. A13-15. Judge Sweeney concluded that the Special Master's analysis on this point was in accordance with the law. A11-13.

Dr. Kerr also provided a number of medical articles, but the Special Master correctly found that none of those articles supported Dr. Kerr's inflammation

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[14] The Special Master also noted Dr. Kerr's testimony that a vaccination, by its very nature, might cause some inflammation. A14. Dr. Kerr, however, did not coherently explain why, if petitioner's vaccination caused "massive microglial inflammation," all her tests for markers of inflammation were negative. A141.

[15] Dr. Kerr opined that there is one very specific condition, central nervous system ("CNS") vasculitis, that can occur without other diagnostic evidence of inflammation. A557-58. He never opined, however, petitioner has this condition and none of petitioner's doctors ever diagnosed her with this condition. A566. Moreover, Dr. Gill testified that she has treated between 20 and 30 patients with CNS vasculitis and "all of them" had other diagnostic evidence of inflammation. A492.

theory. A15. Most importantly, none of the articles addressed the injury suffered by petitioner, a spinal cord stroke. A14-15. The Special Master correctly noted that several of the articles addressed a different condition called "giant cell arteritis" ("GCA") following influenza vaccination. A15. None of the patients developed a spinal cord stroke, nor the extensive inflammatory response alleged by Dr. Kerr that would cause inflammation causing a headache, extremity pain, bradycardia, asystole, and a spinal cord stroke, nor suffered symptoms as quickly as petitioner, all points conceded by Dr. Kerr.[16] A381-82, A384, A387. GCA, Dr. Gill explained, is nothing like a spinal cord stroke and is instead a condition limited solely to the temporal artery and involves strong evidence of systemic immune system inflammation. A15. Finally, none of these articles concluded that the vaccinations discussed actually caused the GCA. See A291 (the authors noted that if an association between the GCA and vaccination was "more than

[16] Petitioner argues that there is at least one case report that suggests that a patient developed GCA "immediately" following a vaccination, which supports her claim. Flores Brief at 47. However, a review of that case report shows that it includes no information on timing other than the use of the word "immediately," when describing the patient's symptoms. A262. The authors actually noted that it was possible that this patient had GCA that began five days *before* he received a flu vaccination. A263. Moreover, Dr. Kerr acknowledged that he could not state that the patient discussed in this report developed symptoms as quickly as petitioner. A393.

coincidental, the mechanism by which [it] exert[s] pathogenic influence remains conjectural"); A213 (noting that while it is possible the flu vaccine may have caused "an autoimmune reaction directed against the temporal artery and clinically manifest as GCA," that "the mechanism by which a [flu vaccine] may induce GCA is unknown"); A263 (noting that "the cause of GCA in our patient remains speculative[.]"). Indeed, when discussing these articles, Dr. Kerr conceded that they only supported a "medically plausible" theory, not a probable one, as required by law. A388.

In short, the Special Master correctly concluded that because none of these articles addressed the injury alleged in this case, they did not provide "persuasive evidence for [Dr. Kerr's] theory." A15. Judge Sweeney found no error with his analysis. A36-38.

4. Petitioner did not provide a reliable medical theory explaining how an HPV vaccination can cause coagulation (blood clots) that can lead to a spinal cord stroke.

The Special Master also appropriately found that petitioner did not present reliable evidence to support Dr. Kerr's final theory that the HPV vaccine can cause platelet aggregation that leads to a stroke. A15. Platelet aggregation occurs when platelets in the blood become sticky and clump together and can lodge in veins or

arteries. Id. The Special Master again considered the testimony from Dr. Kerr and the medical articles he relied upon and found them to be unpersuasive. A16.

First, the Special Master explained, none of the articles referenced by Dr. Kerr supported his opinions. A16-17. Two of the articles discussed reports that several people died sometime after a vaccination. Id. (referencing A266-69, A697-98). The Special Master correctly noted that neither of those articles discussed spinal cord strokes, identified any particular cause of death, discussed any theory connecting a vaccination with a cause of death, mentioned the HPV vaccine, or, most importantly, mentioned the words "platelet aggregation." A16-17. As such, the Special Master concluded that these articles did not constitute persuasive evidence in support of petitioner's claim.[17] Id.

The Special Master also carefully reviewed the remaining articles relied upon by Dr. Kerr, the "Baker article"[18] and the "Rivard article,"[19] both of which

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[17] Dr. Kerr also submitted another article, B. Granel, et. al. *Occlusion de la Viene Centrale de la retin Apres Vaccination contre l' hepatite Virale Par Vaccin Recombinant,* La Presse Medicale (1997) 26: 62-65. A279-83. Petitioner argues that the Special Master should have relied more heavily on this article in his Decision. Flores Brief at 52-53. Notably, at hearing, Dr. Kerr acknowledged that, other than the abstract that was written in English, he had not actually read the entire article because it was written in French. A414-17.

[18] I.A. Baker, et al. *Changes in the heparin neutralising activity of platelet poor plasma after immunisation.* J. Clin. Pathol. 1152 (1979). A181-84.

discuss platelet aggregation. A17. In evaluating these articles, the Special Master credited the testimony of Dr. Gill, as she was the only expert testifying in the area of hematology and had extensive experience in the study and research of blood conditions like platelet aggregation. Id. Dr. Gill explained that both of these studies are very old (30 years old) and do not rely on accurate tests for platelet aggregation. A17, A467-68. She explained that the only reliable way to confirm platelet aggregation is by looking for evidence that platelets are actually "activating and emptying the contents of their granules, which is the hallmark of platelet activation." A468. The tests used to measure coagulation in these articles did not employ that method. Id. Dr. Gill explained that the testing discussed in these articles is so outdated that if submitted for publication today, they would most likely be rejected. A468, A470. Petitioner did not offer any expert testimony to refute Dr. Gill's opinions. A17.

The Special Master found that Dr. Gill's explanation of these articles was simply more persuasive than Dr. Kerr's. A17.

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[19] Georges E. Rivard, et al. *Platelet aggregation induced by swine influenza vaccine*. Lancet. 302 (1977). A260.

5. The Special Master's evaluation of the medical literature was proper and appropriate.

In evaluating the reliability of Dr. Kerr's theories, the Special Master gave substantial consideration to an article relied on quite heavily by both petitioner and the Secretary, the Slade article. A17-20. The Special Master careful reviewed this article and appropriately determined that "it does not offer significant support for Dr. Kerr's general proposition that the HPV vaccine can contribute to strokes." A17. Judge Sweeney held that the Special Master's findings on this issue were in accordance with the law. A33.

The first reason the Special Master discounted the importance of this article is because it is nothing more than a Vaccine Adverse Event Reporting System ("VAERS") survey. A17. Indeed, the Slade authors themselves cautioned that "VAERS data must be interpreted cautiously, and cannot generally be used to infer causal associations." A18 (citing A304-05); see also A754-62. The Court of Federal Claims has repeatedly upheld decisions of special masters who have concluded that VAERS reports do not provide reliable evidence of causation. See e.g. Analla v. HHS, 70 Fed. Cl. 552, 559 (2006) (noting that the CFC "uniformly has upheld the Chief Special Master's concerns about the reliability of VAERS data") (citations omitted); Ryman v. HHS, 65 Fed. Cl. 35, 39-40, 43 (2005)

(affirming a special master's finding that VAERS reports may be biased toward pre-existing notions of adverse events).

Second, the Special Master carefully reviewed the findings of the Slade article and he correctly concluded that it failed to provide persuasive evidence to support petitioner's claim. A19. He correctly noted that the Slade article offered no commentary on spinal cord strokes. Id. He further noted that all of the other types of strokes discussed in the Slade article involved venous thrombotic events ("VTE"), and that petitioner's stroke was most likely an arterial infarct.[20] A19, A302-03. He additionally noted that of the 31 VTEs reported following HPV vaccinations, 90% had other known risk factors for strokes, which would have predisposed these individuals to a stroke absent the vaccination. A19, A302. Finally, the Special Master noted that the VTEs reported had an average onset time of 41.5 days following vaccination, which stands in sharp contrast to the one day onset in this case. A19, A302. For all these reasons, he had ample support for his conclusion that the Slade article did not provide preponderant, reliable evidence that the HPV vaccine can cause spinal cord strokes.

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[20] See discussion of venous versus arterial strokes at section I(A)(2) *supra.*

The Special Master also noted that literature submitted by the Secretary weighed against Dr. Kerr's theories. The first, the "Gold study,"[21] reviewed adverse reports following a total of 5.8 million doses of the HPV vaccine in Australia and found no reports of strokes (either arterial or thrombotic). A21, A143-48. The second article, the "Gee study,"[22] described a large-scale epidemiological study that detected no increased risk of stroke or VTE following HPV vaccination. A21, A311-17. The Special Master acted well within his discretion when he correctly concluded that this literature "adds slightly to the reasons for rejecting Dr. Kerr's causation theory." A21.

B. The Special Master correctly found that petitioner failed to establish a logical sequence of cause and effect pursuant to *Althen* prong two.

The Special Master found, after evaluation of the evidence, that even if petitioner could establish that either of her medical theories was reliable, her claim must still fail because she did not establish a logical sequence of cause and effect

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[21] Michael S. Gold, et. al. *Human papillomavirus vaccine safety in Australia: experience to date and issues for surveillance.* 7 Sexual Health 320 (2010).

[22] Julianne Gee, et. al. *Monitoring of the safety of quadrivalent human papillomavirus vaccine: Findings from the Vaccine Safety Datalink.* 29 Vaccine 8279 (2011).

between her vaccination and alleged injury. A13-16. Judge Sweeney explained that:

> The special master was therefore entitled to conclude that if the logical sequence of cause and effect posited by Dr. Kerr included the existence of inflammation or platelet aggregation, but there was no evidence of inflammation or platelet aggregation in any of petitioner's test results, then petitioner could not establish an essential element of causation linking her HPV vaccination to her spinal cord stroke.

A37. She noted that the Special Master's Decision was in complete *accord* with the Federal Circuit's recent decision in Stone, in which this Court held that even if a petitioner could establish a reliable medical theory explaining how a vaccine could cause a particular injury, absent evidence that the petitioner actually suffers from that injury is fatal to petitioner's claim. A37 (citing Stone, 673 F.3d at 1374). She held that the special master did not err by insisting on "evidence of the biological mechanism by which the [alleged injury occurred]. He merely sought evidence of the existence of the [alleged injury] – a key component of [the expert's theory] – and [the expert] was unable to provide any." A38 (citing Stone, 673 F.3d at 1385); see also Hibbard v. HHS, 698 F.3d 1355, 1365 (Fed. Cir. 2012) (when a petitioner alleged that her vaccine caused an autonomic neuropathy, which in turn caused disautonomia, but failed to present reliable evidence that she actually had any medical evidence of the predicate condition, an autonomic neuropathy, her claim fails under Althen prong two). As such, Judge Sweeney explained that even

if petitioner were able to establish the reliability of any of her alleged theories of causation – inflammation or coagulation – which she has not, her evidence still fails because she did not demonstrate that she has any evidence of inflammation or blood clotting. A38. A review of the evidence considered by the Special Master demonstrates he properly exercised his authority. A36-38.

First, the clinical record fails to support petitioner's inflammation theory. The Special Master correctly noted that petitioner was tested many different times for signs of systemic inflammation and every test was normal. A14. As Dr. Gill explained, patients that have systemic inflammation have "elevated white blood [cell] counts [WBC] . . . an increase in neutrophils . . . an increase in monocytes . . . [an] elevated SED [(erythrocyte sedimentation rate)], an elevated C-reactive protein, and an elevated platelet count," so if petitioner were experiencing inflammation, her test results would have revealed her condition. A457-58. All tests for inflammation ordered immediately upon petitioner's first arrival at Mt. Sinai Hospital – WBC, platelets, and neutrophils – were all within normal limits. A459. When she was transferred to Rush Hospital, her SED was reviewed, and it was perfectly normal. A461-62. A test for C-reactive protein was negative. A462. Dr. Bingham also explained that testing of petitioner's spinal cord fluid showed no signs of inflammation. A14. For these reasons, even if petitioner had

presented a reliable theory that the HPV vaccine could cause inflammation that could ultimately lead to a spinal cord stroke, which she did not, her claim must still be denied because she failed to present preponderant evidence that she actually had any clinical signs of inflammation immediately after her stroke. A14.

Next, the Special Master correctly noted that petitioner underwent a number of tests that looked for platelet aggregation, and none was found. A15-16. Just a few hours after petitioner's onset in symptoms, her platelets levels were checked and were completely normal. A16, A458. Dr. Gill also noted that additional coagulation testing was performed within hours of the onset of petitioner's symptom onset – prothrombin ("which refers to some of the clotting factors in the blood") and activated partial prothrombin time (which "screens for the presence of some of the clotting factors in the blood") were also perfectly normal. A460. Dr. Kerr did not point to any clinical tests that suggested any evidence of abnormal coagulation in petitioner at any point following vaccination. A16-17.

Third, petitioner also failed to present any evidence on what Dr. Kerr opined was "absolutely critical" in all of his theories – that petitioner had a genetic predisposition that made her susceptible to blood clotting that could lead to a stroke. A11.

In short, the Special Master correctly found that the record lacks evidence that is necessary for petitioner to establish a logical sequence of cause and effect under her proposed theories.

C. Petitioner failed to submit preponderant evidence that her stroke occurred within a temporally appropriate timeframe under *Althen* prong three.

Althen prong three requires "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352.

Here, the Special Master found that petitioner submitted no reliable evidence that a vaccination could cause inflammation that could result in a stroke within 24 hours of vaccination. A23-24. He noted that Dr. Gill, who has extensive experience in treating patients with immune-mediated blood disorders, opined that it would take at least four days for inflammation to develop. A14, A24. He noted that while Dr. Kerr argued that a one-day onset was appropriate, Dr. Gill's opinions were supported by two of petitioner's treating doctors. The first, Dr. Tilwalii, noted that petitioner's "vaccination 1 day prior is too close to onset of [symptoms] to induce an inflammatory response." A5-6 (citing A685). The second, Dr. Stefofski noted that petitioner's rapid onset in symptoms "strongly

favors a vascular etiology over immune mediated/inflammatory (definitely too soon for [her HPV vaccine to be a] myelitogenic trigger)." A6 (citing A686).

Petitioner argues that the Special Master erred, as a matter of law, by interpreting the statements of Drs. Tilwalii and Stefofski to mean that the HPV vaccine could not have induced an immune-mediated inflammatory response within 24 hours. Flores Brief at 29-33. However, petitioner can point to no evidence in the record that the Special Master's reading of these statements was unreasonable. Indeed, the Special Master took these statements at their face value and found that they did not lend support to petitioner's claim. Simply because petitioner believes there may be other reasonable interpretations of petitioner's medical records does not constitute legal error. As a matter of law, a special master's factual determinations must be sustained unless it is found that they are "wholly implausible," or otherwise not based on the factual record. Cedillo, 617 F.3d at 1338 (citing Lampe, 219 F.3d 1363). Because petitioner cannot demonstrate such error her, the Special Master's findings must be affirmed.

Based on this evidence in the record as a whole, the Special Master reasonably concluded that petitioner had not met her burden under Althen prong three.

CONCLUSION

Petitioner has not shown that the Special Master applied an incorrect legal standard, or that his evaluation of the evidence was arbitrary and capricious, an abuse of discretion, or otherwise not in accordance with the law. Laid bare, petitioner simply disagrees with the Special Master's well-supported findings, and seeks an opportunity to retry her case, which is not permitted. Hazlehurst v. HHS, 604 F.3d 1343, 1349 (Fed. Cir. 2010). Therefore, the Secretary respectfully requests that the Court uphold the opinion of the CFC affirming the Special Master's Decision.

Respectfully submitted,

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CERTIFICATE OF COMPLIANCE

I hereby certify, based on the line count of the word-processing system used to prepare this brief, that the brief contains 9,572 words and 864 lines of text, and is, therefore, in conformity with Fed. R. App. P. 32(a)(7)(B).

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CERTIFICATE OF SERVICE

I hereby certify that on this 31st day of July, 2014, the foregoing **BRIEF OF RESPONDENT-APPELLEE** was served electronically upon:

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